"Navigate GMP with DBA"*

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# DUE DILIGENCE

## Obligations of the pharmaceutical contract giver[1]

### Due diligence is:

- The way to discover everything before you buy;
- The process of investigation, performed by contract givers (or their appointed agents), into the details of a potential contract acceptor, such as an examination of operations and quality management and the verification of material facts;
- The process of checking the accuracy of information contained in a company public statement, such as a Site Master File or TGA licence, before recommending that company as a contract acceptor; and
- The act of one company investigating another company before buying its products.

Due diligence tests the information provided, to determine if assumptions being relied upon are correct, and ultimately to check if what one is intending to buy is as it is supposed to be.

Due diligence is the level of judgment, care, prudence, determination, and activity that a person would reasonably be expected to do under particular circumstances. Applied to pharmaceutical manufacturing, due diligence means that contract givers shall take all reasonable precautions, under the particular circumstances, to ensure that the goods produced by the contract acceptor are fit for their purpose.

To exercise due diligence, a contract giver must put into operation a plan to identify possible risks and carry out, or ensure the contract acceptor carries out, the appropriate corrective action to prevent accidents or injuries arising from these hazards.

"Quality" due diligence involves going beyond publicly available information. It goes behind the statements presented in the Site Master File or on the TGA licence and assesses whether quality management is sustainable, whether production can be maintained to the standard specified, and whether commercial agreements have value.

The pharmaceutical contract giver must be able to demonstrate due diligence in the selection of the contract acceptor, EVEN IF the contract giver is not the holder of a TGA licence. Due diligence strategies are now a key component of good corporate governance and risk management. The contract giver needs to identify and manage the risks in manufacturing, even if they do not have technical expertise or are relying on the contract acceptor's experts. Risks need to be foreseen and strategies adopted to manage them effectively.

### Trust but Check and Verify

Senior management needs to benchmark operational and compliance performance and keep abreast of best practices. Due diligence should entail pre-contract assessment including a technical audit, contracted if necessary to an expert if the contract giver does not have the expertise. Not having any expert employed within the contract giver's firm is not an excuse for not ensuring a technical due diligence audit is carried out. There are many competent firms who specialise in this work. Use them!

[1] Contract manufacture means the manufacture in part or whole of a product by one (or more) manufacturers, the Contract Acceptor, for another party, the Contract Giver (1990 Australian Code of GMP)

 

The due diligence assessment of Quality Assurance and Manufacturing systems of the company under consideration is a crucial step in pre-contract negotiations. Such an exercise enables identification of various risks and liabilities, and provides valuable information to assist purchase price negotiations.

The contract giver must:

- Identify and assess the significance of an contract acceptor's risks;
- Assist in developing strategies to eliminate or minimise risks;
- Conduct formal audits or inspection using trained experts (it is an inspection, not a visit!); and
- Train personnel in practices designed to enhance the management of identified risks.

Due diligence provides protection, assurance and objective reporting during the contract giving processes. Critical elements of the due diligence process includes:

1. Historical performance – check previous TGA audit reports, check internal audit reports, check deviation and fault analysis, check out of specification results, etc.
2. Current position - gaps
3. Risks
    a. Identify the risks
    b. Prioritise the risks according to objectives
    c. Recommending stratagies to minimise risk
    d. Map the risk
    e. Develop a risk register
    f. Regularly monitor for risks – periodic, planned audits are needed.
4. Ensure there is demonstrable corrctive action prior to contract being placed – seek objective evidence not just reassurances.

GMP due diligence audits test compliance with cGMP, statutory, and the Manufacturing Principles, introduces responsibility and enables GMP performance to be analysed.

Due diligence inspections shold be conducted according to written protocols or against written project-specific criteria.

Check and verify:

- Assessment of compliance with: legislation, standards and guidelines (a HACCP plan is ideal);
- corporate policies and project commitments;
- technical and environmental processes and constraints;

## Specific objectives of due diligence investigation:

- Conduct
    - interviews with site personnel
    - inspection of facilities
    - review of documentation
    - Quality monitoring data
- Assess efficacy of GMP management programs and systems
- Identify and assess short- and long-term GMP liabilities, risks and hazards

The conditions for establishing due diligence includes at least these criteria:

- The contract giver must have in place written policies, practices, and procedures. These would demonstrate that the contract giver carried out GMP audits at the contract acceptor, identified unsafe practices and hazardous conditions and made necessary changes (or ensured that the contract acceptor made necessary changes) to correct these conditions;
- The contract giver must provide the appropriate training and education to the contract acceptor so that it can understand and carry out production and quality control according to the established policies, practices, and procedures.
- The contract giver must monitor the contract acceptor and ensure that the contract acceptor is following the policies, practices and procedures.
- The names of the persons on the manufacturing licenses at both the contract acceptor and the contract giver have a duty to take reasonable care to ensure the MPs are followed.
- The contract giver should document, in writing, all of the above steps: this will give the contract giver a history of how the contract acceptor's program has progressed over time.
- Maintain due diligence through a number of vetting, authentication and tracking services, such as independently checking the contract giver's production by means of , for example, samples of products sent to third party quality control testing for verification of the contract giver's certificates of analysis, follow-up audits, etc.

All of the elements of a "due diligence program" must be in effect before any contract is given. If the contract giver has questions about due diligence, they should seek expert advice for their situation to ensure that all appropriate due diligence requirements are in place.

## Example clauses for a GMP contract **(always seek legal advice on any contract!):**

**FACILITY ACCESS** (Contract giver), through its employees, consultants or other representatives will have the right during normal business hours and at a time mutually agreed to inspect (Contract Acceptor's) manufacturing operations to determine whether or not (Contract Acceptor's) is complying in all respects with its obligations hereunder. (Contract giver) warrants that all such inspections and audits shall be carried out in a manner calculated not to unreasonably interfere with (Contract Acceptor's) conduct of business and to insure the continued confidentiality of (Contract Acceptor's)business and technical information. Further, (Contract giver) agrees to comply with all of (Contract Acceptor's) safety and security requirements during any visits to the (Contract Acceptor's) facilities. Following an inspection which will in any way affect the production of Product for supply to (Contract giver) by the TGA, FDA or any other European Community authority (as set forth on attached), (Contract Acceptor's) will notify . (Contract giver) in writing of any material issues that may be pertinent to the supply of Product to (Contract giver). The parties agree to cooperate in good faith and engage in an active dialogue in an effort to resolve any issues resulting from any such inspections.

## Q and A

**Q For contract manufacturing, is an audit required if the contract giver has on-site representatives during all the manufacturing at the contractor's site?**

**A** An audit of a contractor should be used to "qualify" the contract acceptor for specific operations, even if there are contract giver's representatives on-site during manufacture.

**Q**. **What recourse does a contract giver have when the contract manufacturer does not allow audits?**

**A** Section 16.13 (FDA CFR) says: "The contract should permit a company to audit its contractor's facilities for compliance with GMP." In cases where the contract manufacturer refuses to be audited, it cannot be your partner anymore.